An Update of the NIOSH Nanotechnology Research Program

University of California, School of Public Health
Nanoparticle Safety Symposium
July 29, 2009

Charles L. Geraci, Ph.D., CIH

National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention

Objectives

- Provide updates on critical work in NIOSH
- Share what has been learned
- Discuss results and products
- Identify future work
- Discussion

Unless you've been living with this guy,

you realize that nanotechnology is poised to impact many arenas.

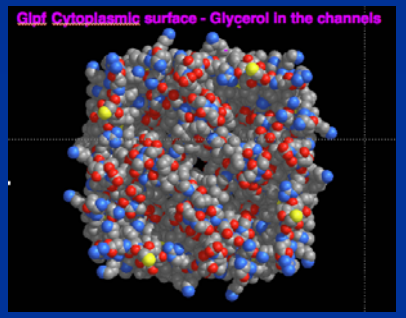
Nanotechnology and Occupational Health

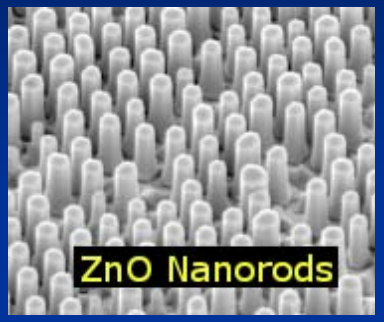
- Nanomaterials are purposely engineered for their unique, size-dependent properties and behavior.
- Do these new 'nano' materials present new safety and health risks?
- How can the benefits of nanotechnology be realized while proactively minimizing the potential risk?

The Focus: Free Engineered Nanoscale Particulate Matter–"Nanoparticles"

- Not firmly attached to a surface
- Not part of a bigger item (e.g., microchip, cell wall)
- Can result in exposure via inhalation, skin absorption or Ingestion

Issue for inhalation: agglomerated ENP has the activity of the primary ENP





The Current Hazard Picture

- More reactive: Chemically and biologically
- Nano-form of ‘familiar’ materials and new nanomaterials being evaluated
- Base of knowledge is building rapidly
- First and greatest exposure potential is in the workplace: labs, scale up, production, use
- EHS issues remain the top challenge to commercialization (Industry survey of business leaders)

What is needed?

A proactive, prudent, protective approach – good risk management.

Evaluating Hazard and Managing Risk

A collaborative effort between:

- Researchers: understand new materials and hazards
- Business alliances: foster knowledge and collaboration
- Manufacturers: responsible practices and communication
- Users: Follow good practices
- Risk managers: provide HS&E guidance

NIOSH Research

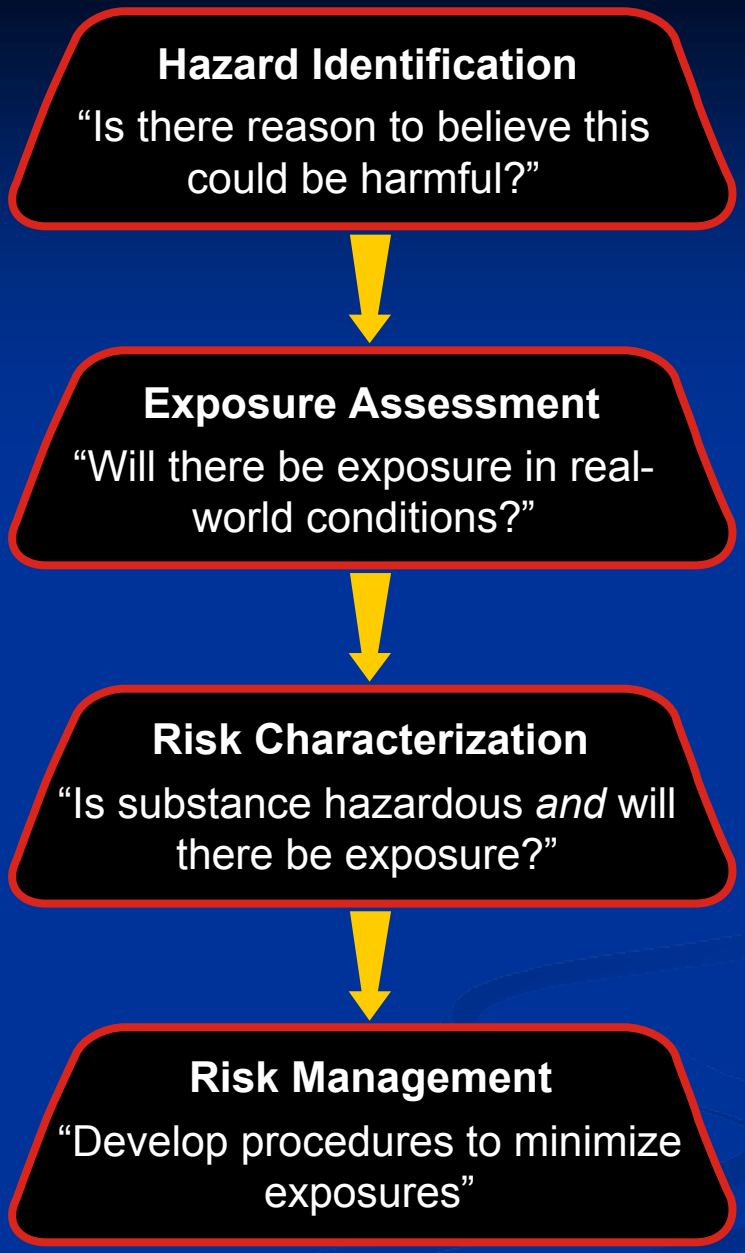
- Toxicological Research
- Safety Research
- Epidemiology and Surveillance

- Field Assessment
- Material Characteristics
- Process Characteristics
- Process Descriptions
- Work Practices

- Risk Assessment- Dose /Duration
- Dose Modeling
- Exposure Characterization

- Risk Communication
- Control Technology Research
- PPE
- Medical Surveillance
- Information Dissemination

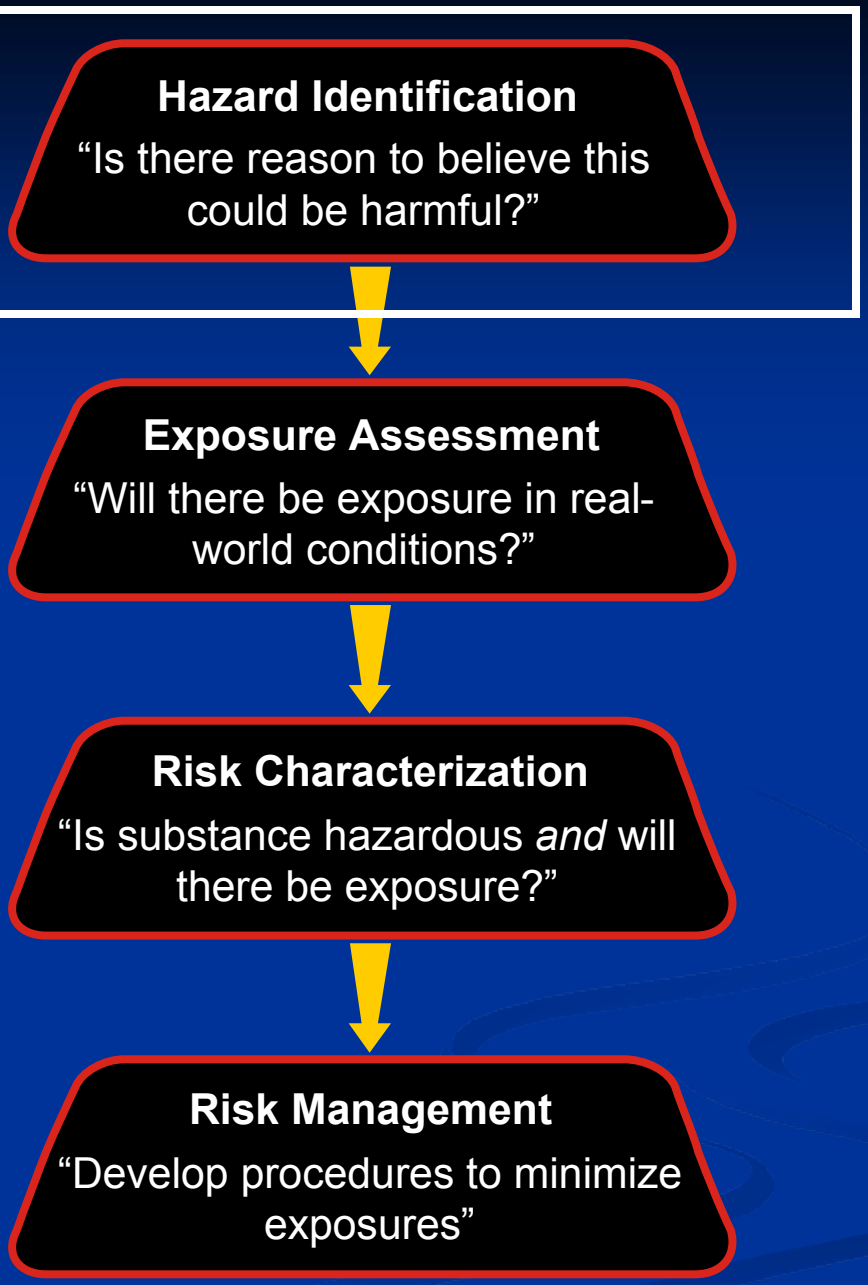
Risk Management Model



Key Elements of Risk Management

Hazard

Nanotoxicology
What do we know?
Are there 'trends'?



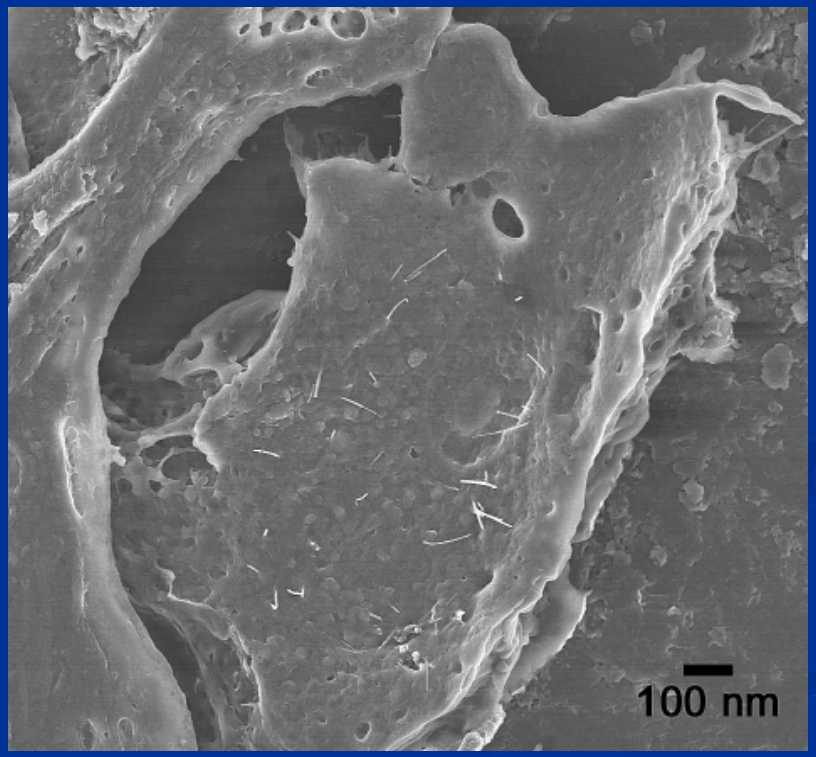
NIOSH Nanotoxicology Summary

- Nanoparticles under investigation
  - TiO_2, CB, SWCNT, MWCNT, metal oxides, nanowires, and nanospheres
- Target organs
  - lung, skin, brain, cardiovascular system
- End points
  - inflammation, oxidant stress, fibrosis, translocation
- Dose Metrics
  - Surface area
  - Correlate mass, size distribution and number

Nanotoxicology: SOT 2009

101 Papers/Posters on Nanotoxicology

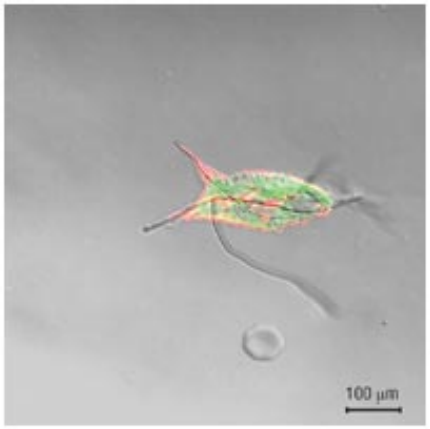
- **37 Carbon-Based Nanomaterials**
- **24 Carbon Nanotubes**

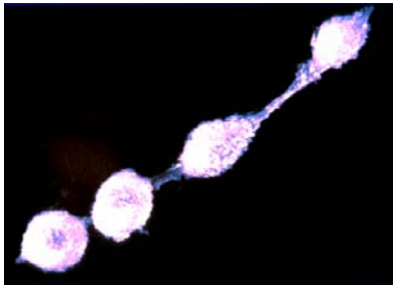


Courtesy of
R. Mercer, NIOSH

Current Research Results

Nanoparticle Toxicity to Respiratory Tract





Rat lung cells cannot digest and clear long carbon nanotubes.

D. Brown, Napier Univ. and I. Kinloch, Univ. Manchester

Effects of SWCNT following aspiration and inhalation:

- Rapid but transient lung **inflammation**
- Agglomerates produce **granulomas**
- Dispersed structures produce progressive interstitial **fibrosis**

Shvedova et al. the Toxicologist 102: A1497, 2008

Intraperitoneal injection of MWCNTs:

- Pathogenic behavior related to length
- Inflammation and formation of granulomas
- Long CNT fibers more active than short fibers or bundles
- Mimics the same processes as asbestos ?

Poland, et al: Nature Nanotechnology, May, 2008

Current Research Results

Nanoparticle Toxicity to Respiratory Tract (Cont.)

Hubbs, Mercer et al; SOT 2009: Pharyngeal aspiration of MWCNT

- MWCNT Penetrate the pleura
- Persistent inflammation and fibrosis

-"Preliminary findings that justify further research"-

Sager, Castranova et al; SOT 2009: Fate of UF TiO2 v. F TiO2 following installation in rats

- Suggestion that Ultrafine (Nano) TiO2 migrates more readily to the interstitium than Fine TiO2.

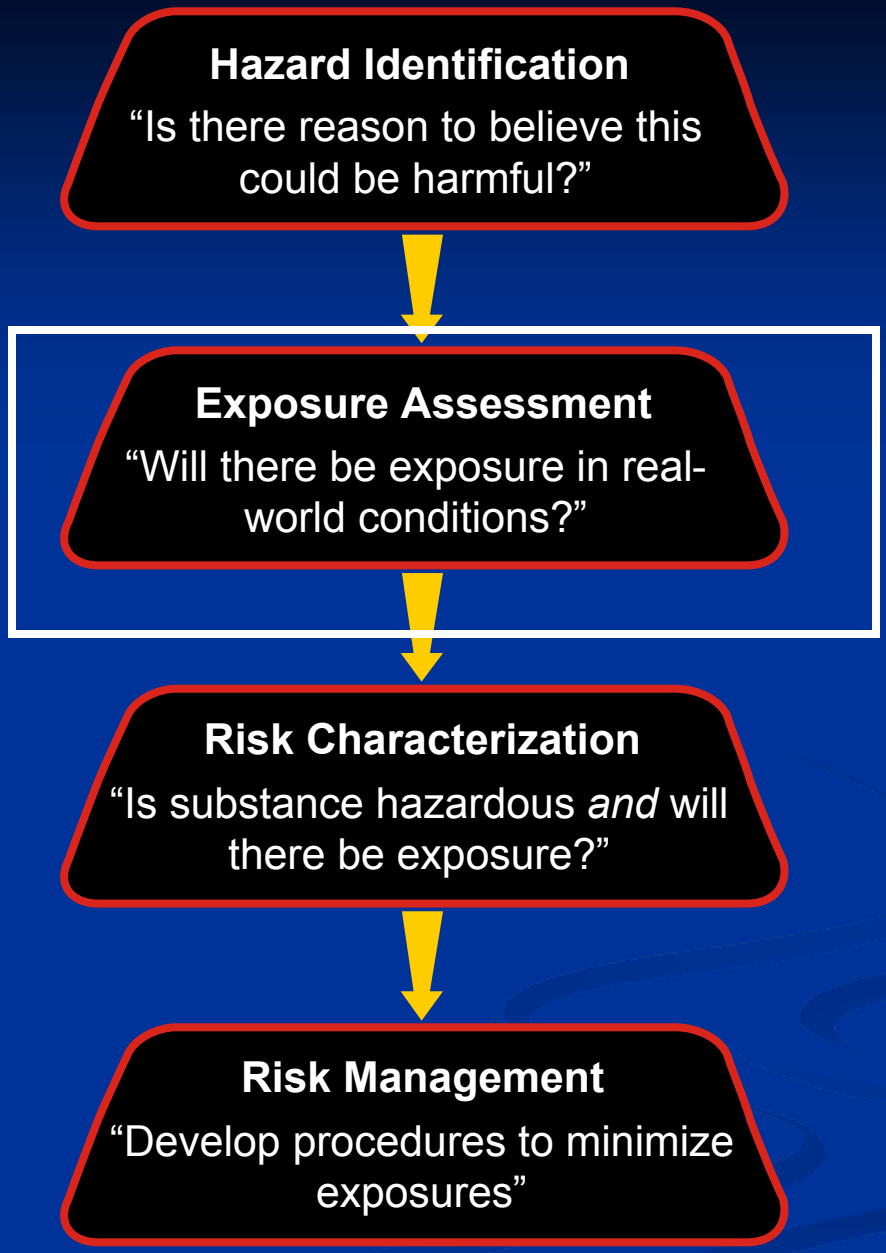
Schaeublin et al; SOT 2009: Differential cytotoxicity observed in gold nanospheres and nanorods

- Human keratinocite cells treated with Au spheres and rods
- Cell viability and membrane integrity evaluated
- Rods more toxic at lower doses: **shape matters**

Key Elements of Risk Management

Exposure →

Can it be measured?
Where is it occurring?
Metric?

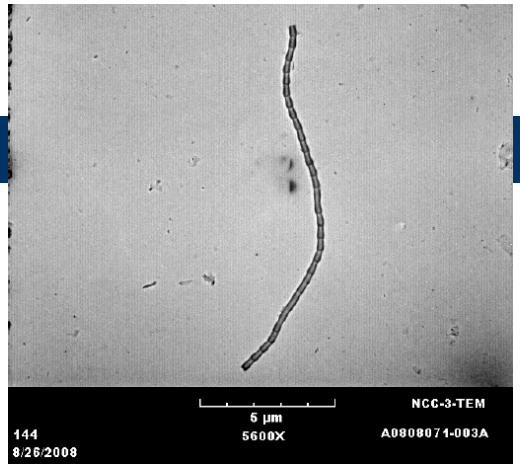


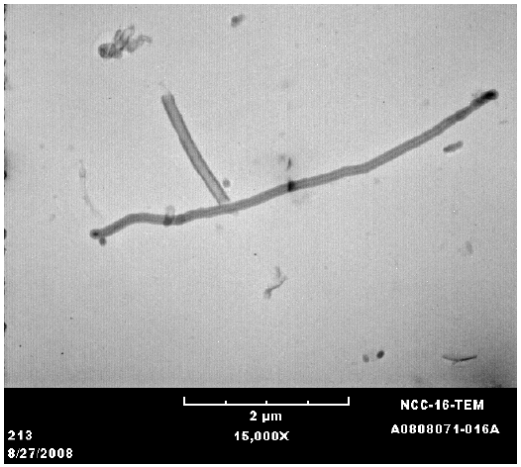
Can nanoparticles be measured? Sure.

Mention of any company or product does not constitute endorsement by NIOSH

Exposure Scenarios Evaluated

Correlate Simple and Complex Measurements





Particle Counters

TEM and
Elemental analysis

Nanomaterial Emission Assessment Technique

Production System OFF → Measure background particle number concentrations at 3 to 5 locations with a CPC and OPC

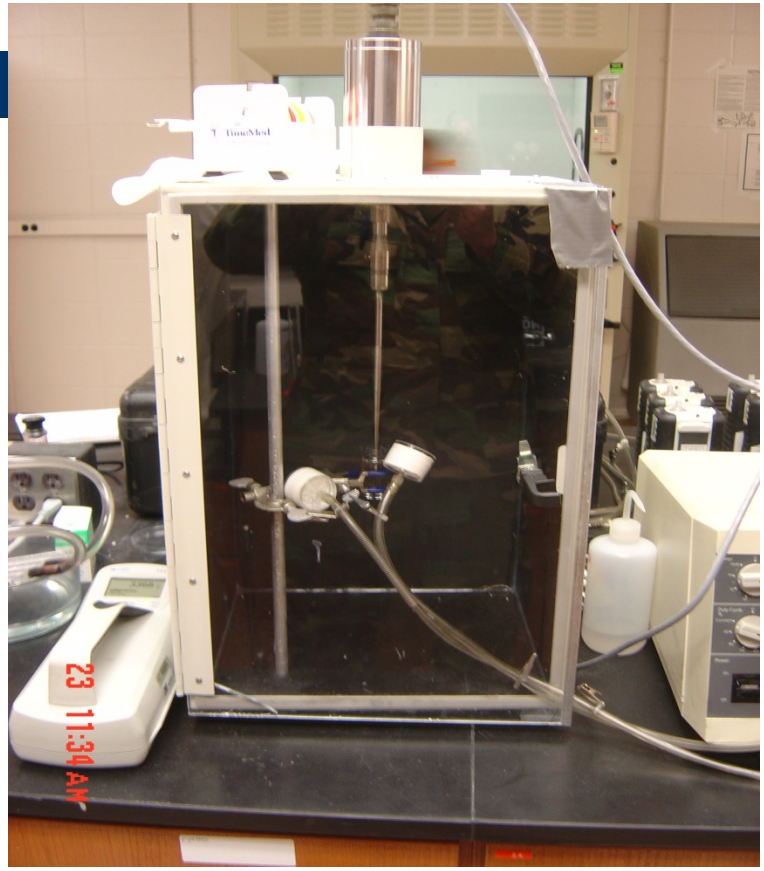
Turn Production System ON → Repeat particle number concentration measurements at suspected emission points

Are particle number concentrations with the productions system ON higher than average background particle number concentrations with the system OFF?

YES → Collect co-located open-face air filter samples for TEM and analytical analysis at locations of possible emissions identified by the CPC and OPC. Collect a second set away from the process to use as background samples.

NO → Controls appear to be adequate
No further testing is necessary

Examples of Sampling Strategy



Field Assessments

- 2006 - 3 facilities
- 2007 - 8 facilities
- 2008 - 7 facilities
- 2009 - 3 facilities

Example particle number concentration data from CPC

Area	Particles/cm^3
Background (CNT)	1,246 –19,500
Weighing of CNT inside of hood, hood turned off	1,476
Opening of CNT CVD reactor	42,400 (controls off) 998 (controls on)
Silica Iron compound	79,700 (inside spray booth) 2,300 (outside spray booth)

Example particle number concentration data from CPC

Area	Particles/cm^3
Inside a class 100 clean room	0
Shopvac with no filter	80,700
Shopvac with HEPA filter	0
Propane powered forklift	45,021
Electric arc welding	84,590

NEAT - Initial Assessment

- Limitations
  - Background fluctuations and other “incidental” sources of nanoparticles
  - TEM sensitive to filter loading
  - Area versus personal breathing zone monitoring

Lab Scale Using Local Exhaust

Ventilated enclosure used to control potential emissions during destructive sample testing of electrospun nanofiber on a cellulose substrate.

Particle counts used to measure possible releases during testing. Counts outside enclosure were not significantly above background.

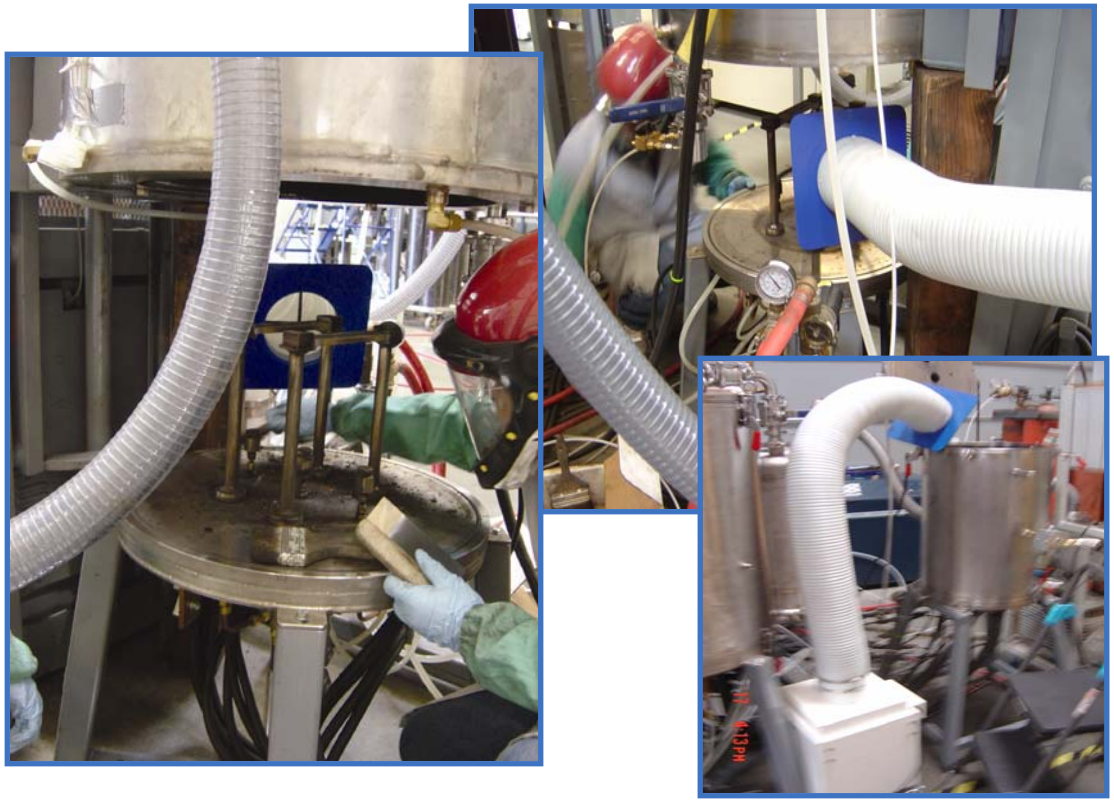
Courtesy of Mark Methner, PhD, CIH

Larger Scale

Mixing of carbon nanofibers inside ventilated enclosure (face of opening is covered in plastic strips for easy access). Air is drawn underneath plastic strips and up to ceiling exhaust vents.

Courtesy of Mark Methner, PhD, CIH

Case Study: Use of LEV during reactor cleanout



Next version…

Average percent reduction from the use of a local exhaust ventilation unit
96 +/- 6% based on particle counts
88 +/- 12% based on mass

Mark Methner, PhD, CIH; JOEH June 2008

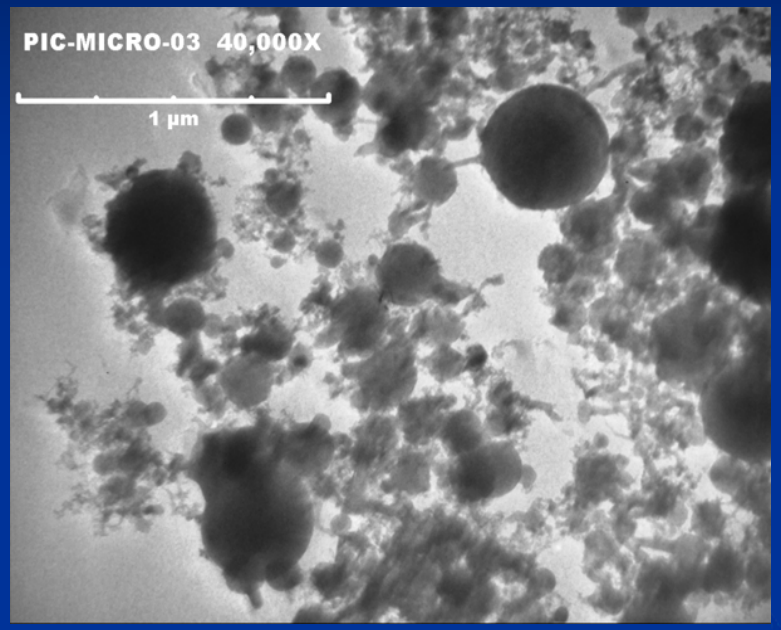
Field Studies: Findings

- Workplace exposures do occur: R&D to manufacturing
- Exposure assessment methods require experience and careful interpretation
- Control methods are effective for many processes
- Guidance based on good risk management principles is effective

Challenge: Move from Simple to Complex Measurements

Starting Point

Mass, Size Distribution, Surface Area, Etc.



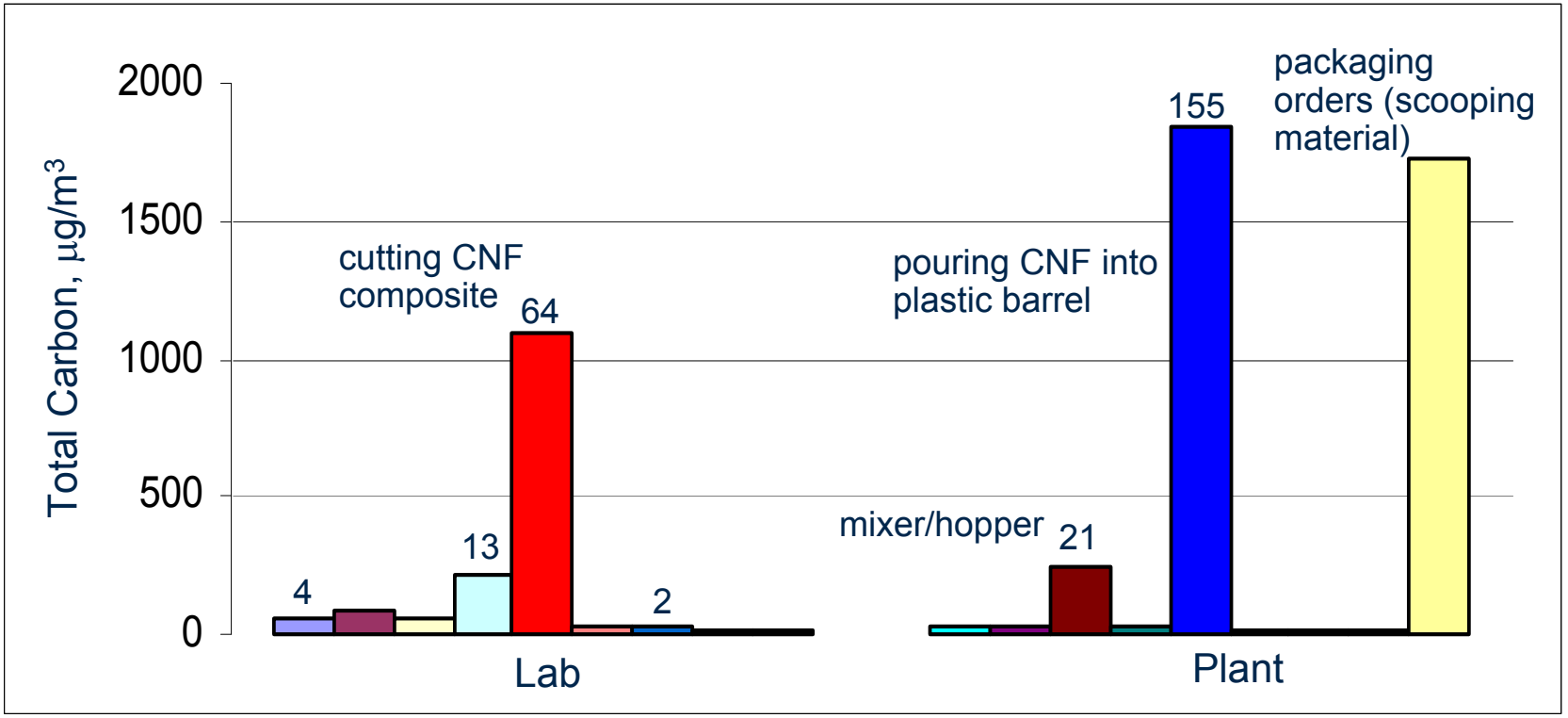
TEM analysis of aerosol

Good **Better** **Best?**

Examples of NIOSH Field Investigations

Type of Facility	Type of Particle, Morphology	Size of Particle	Range of "Potential" Exposure Concentrations
University Research lab	Carbon Nanofibers	Approx. 100 nm diameter, 1-10 microns long	60-90 µg/m^3
Metal Oxide Manufacturer	TiO_2, Lithium Titanate, powder	100-200 nm	<100 nm: 1.4 µg/m^3 (TiO_2) Total dust: 4-149 µg/m^3 (TiO_2) <100 nm: ND (Li) Total dust: ND -3 µg/m^3 (Li)
Manufacturer	Carbon Nanofibers	Approx. 100 nm diameter, 1-10 microns long	15 - 1800 µg/m^3
Research and Development lab	Quantum Dots, spheres	2 -8 nm	ND
Metal Oxide Manufacturer	Manganese, Silver, Nickel, Cobalt, Iron oxides, spheres	8 -50 nm	67 - 3619 µg/m^3
Research and Development lab (Pilot-Scale)	Aluminum, spheres	50 – 100 nm	40 - 276 µg/m^3
Research and Development lab	Elemental Metals - Silver, Copper, TiO_2	15 – 40 nm	ND
Filter Media Manufacturer	Nylon 6 Nanofiber	70 - 300 nm diameter, continuous length	ND

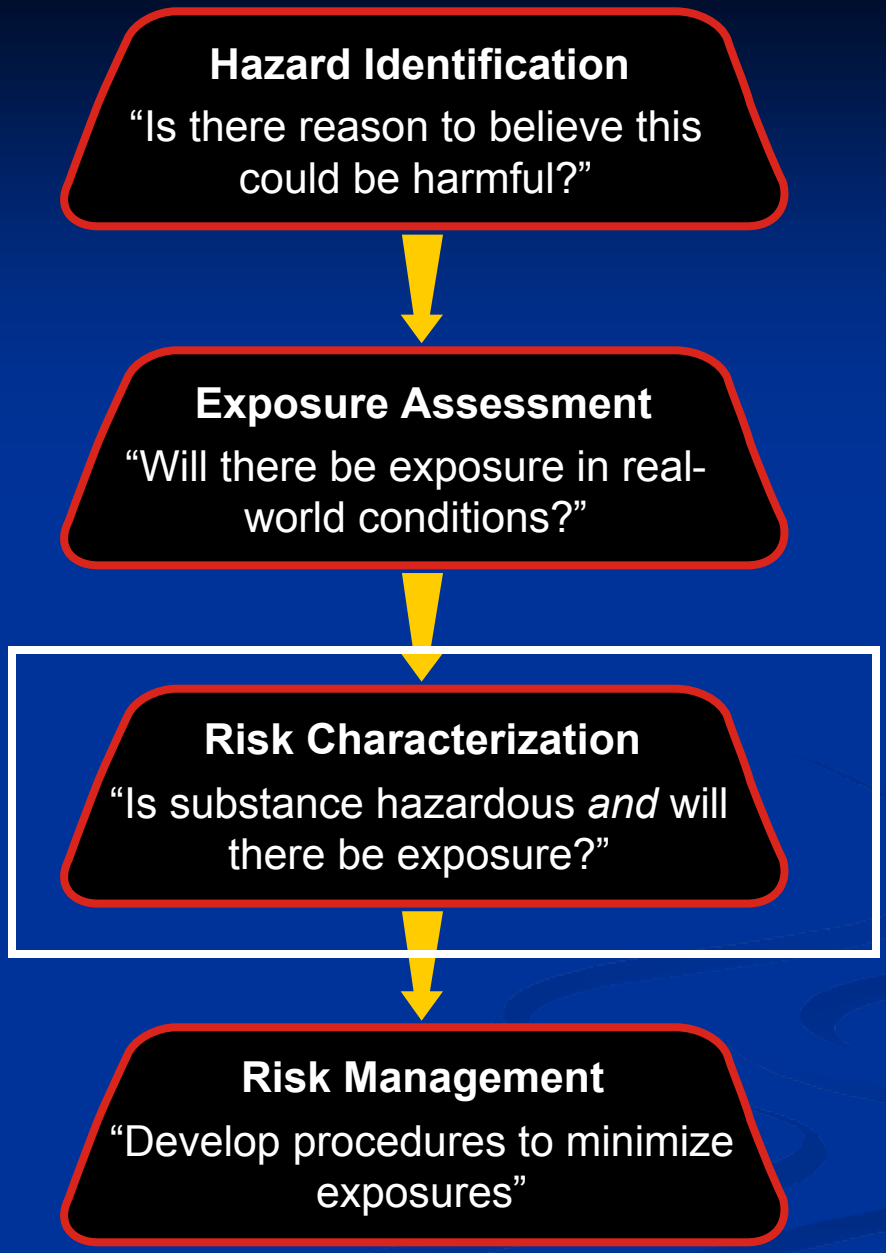
CNF Air Sampling Results as Total Carbon (µg/m3)



Key Elements of Risk Management

Risk

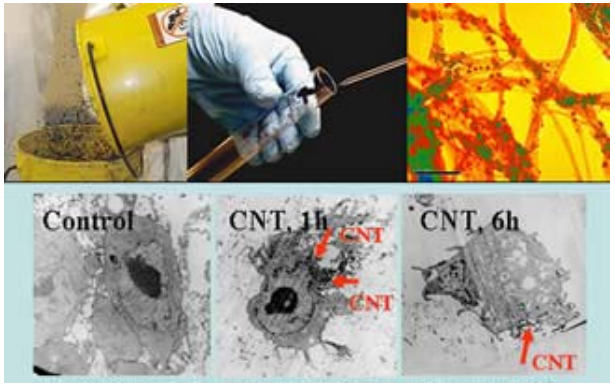
Hazard x Exposure.



Hazard and Risk Picture - Carbon Nanotubes

- SWCNTs more fibrogenic than an equal mass of ultrafine carbon black or fine quartz.
- Doses approximated exposure at the PEL for graphite (5 mg/m3) for 20 days
- MWCNT can penetrate the pleura – more data needed

Message: The PEL for the 'large' form of a material may not be a good guide for the nano form.



Graphics courtesy of Andrew Maynard and Anna Shvedova

Risk Assessment: Ultrafine (Nano) TiO_2

NIOSH draft recommended exposure limits (RELs):

- 1.5 mg/m3 fine TiO2;
- 0.1 mg/m3 ultrafine TiO2
- Reflects greater inflammation & tumor risk of ultrafine on mass basis

Same message: The OEL for a material in its 'large' form may not be appropriate for the Nano form

Framing the Hazard Picture

Based on what is known, how would we describe the hazard and the control needed?

More active than 'bulk form' ⇒ Next level up

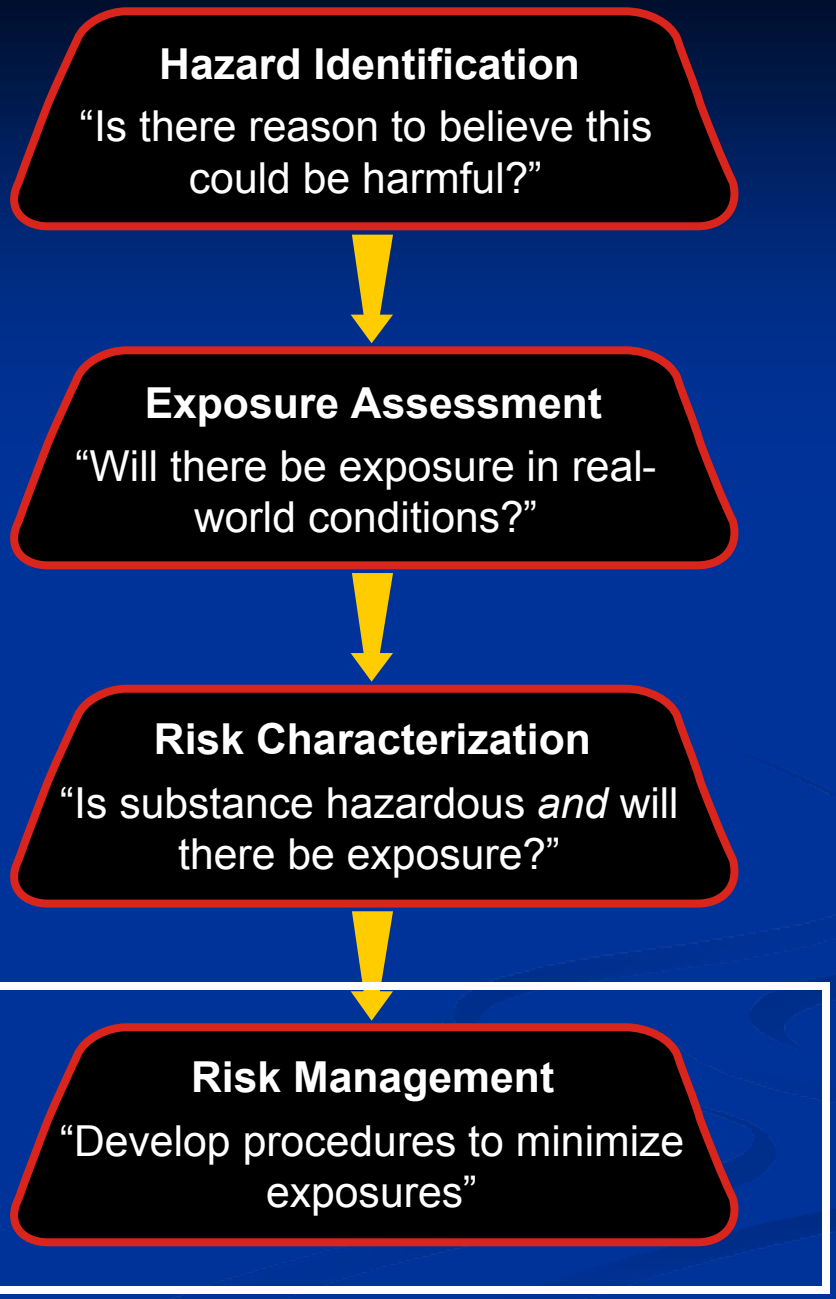
CNTs more active than TiO2 ⇒ Different controls

Is this how the hazard picture is shaping up?

"Dust" TiO2 NanoTiO2 Metals NanoMetals CNT Other ENP?

Less **More**

Key Elements of Risk Management



Recognize and Manage Risk

Tools?
Help??

Tools for Risk Recognition and Management

- Hazard communication
  - MSDS: Often the primary source
  - Supplier information
  - “Literature”
- Process evaluations: Stewardship
- On-Site assessments

MSDS for Nanomaterials: Effective?

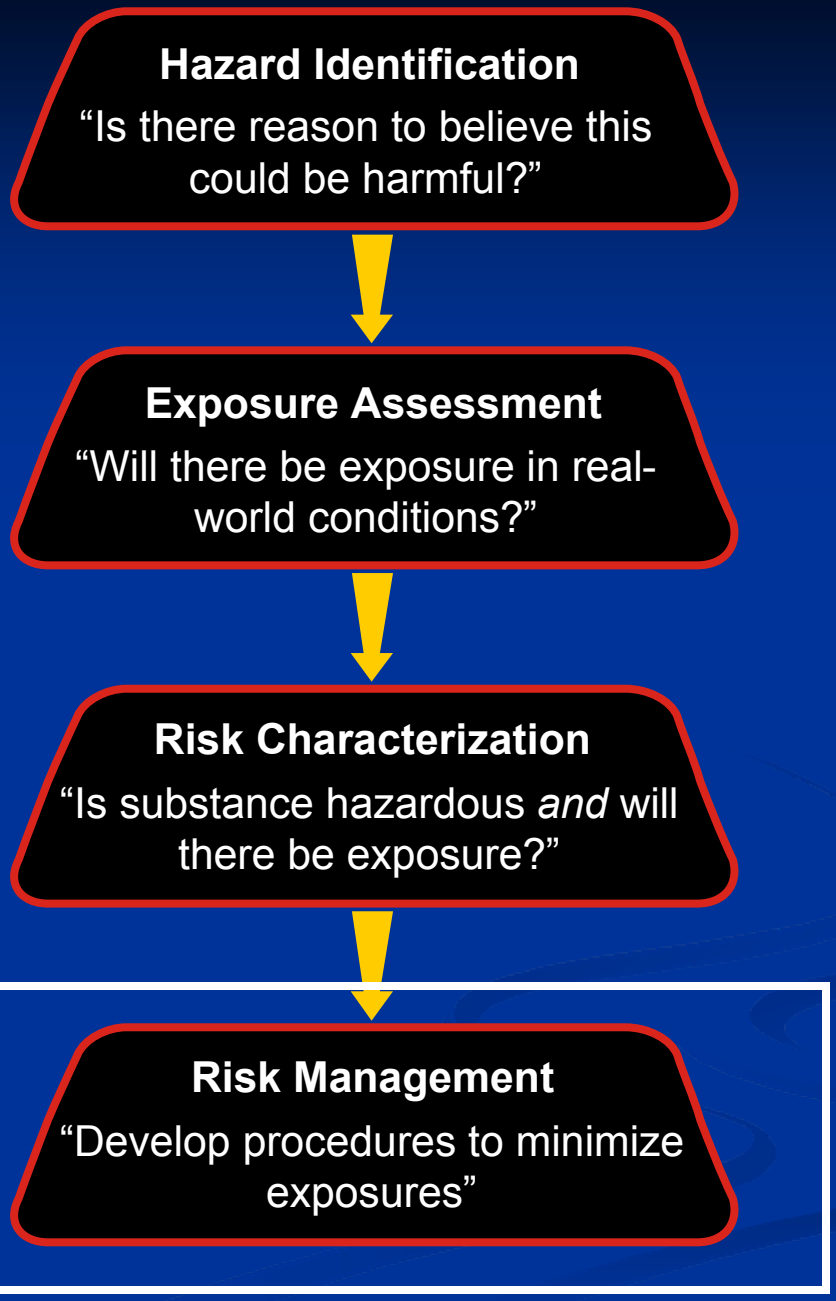
Case Study by NIOSH (AIHce 2009 Presentation)

- 60 MSDS's for Nanomaterials reviewed.
- 58% referred to the PEL for bulk material
- 80% did not provide size information
- 87% did not contain toxicological data specific to the nanomaterial.

Detailed information was presented at AIHce

Work needed!

Key Elements of Risk Management



Controls

What works?
What has been used?
What can be reapplied?

Key NIOSH Research: Controls

- Conventional controls appear efficient
- Special attention to controls for CNTs
- Pharma approach a good model
- Filtration: HEPA filters are efficient for nanoparticles
- Respiratory Protection: NIOSH Certified N95 and P100 respirators provide protection

What we know

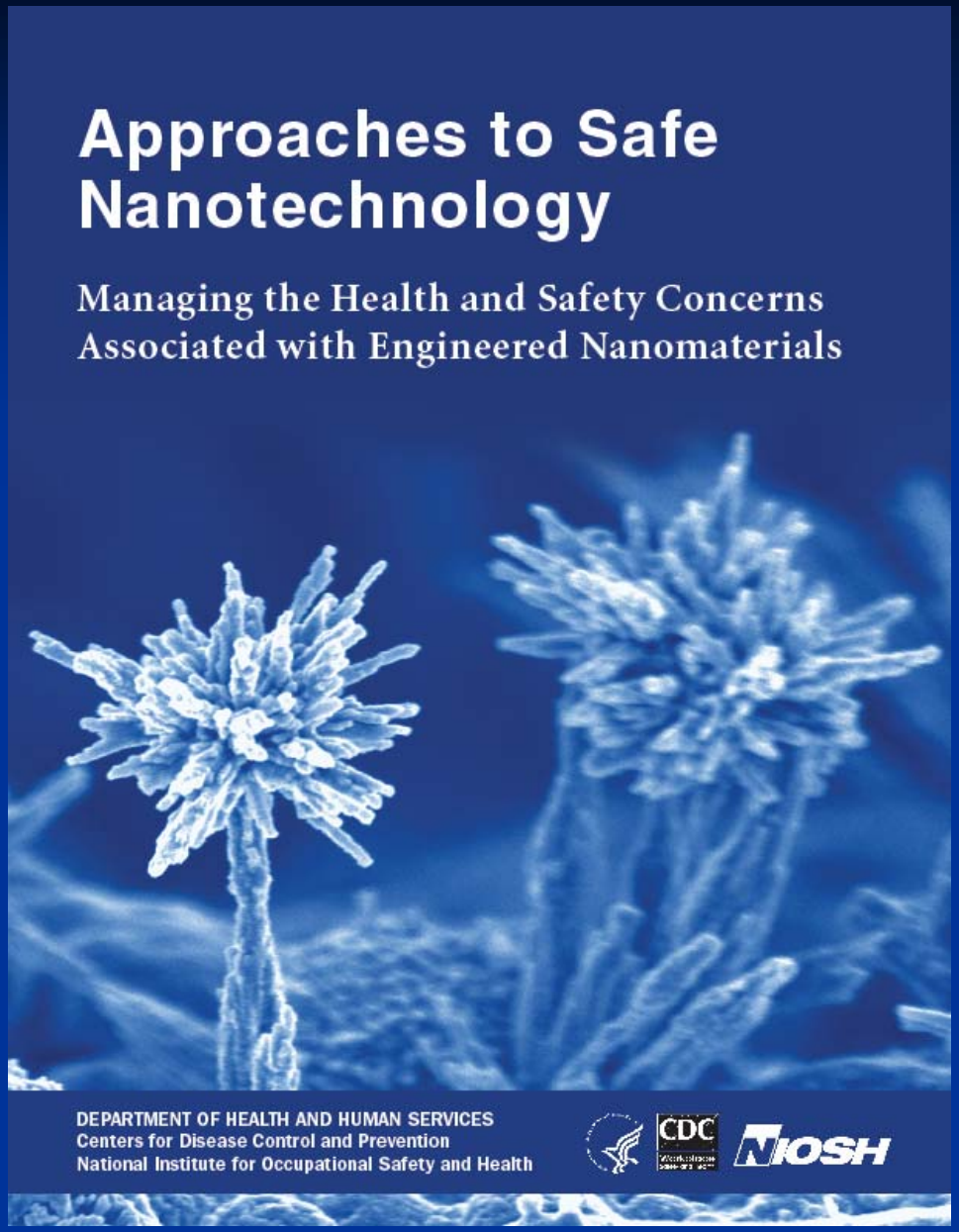
- Some potential hazard
- Some exposure occurs
- Some risk may exist
- Nanoparticles can be measured
- Nanoparticles can be controlled
- Filters and respirators should protect
- There are no specific exposure limits
- No specific medical tests, but hazard surveillance is prudent

What we don't know

- Nature and extent of hazard
- Nature and extent of exposure
- Nature and extent of risk
- What measures to use
- Limitations of controls
- Limitations of protection
- What limits are appropriate
- Content of surveillance

Key NIOSH Contributions

- Develop and disseminate guidance
- Research results in support of a Risk Management approach
- Communicate findings
- Collaborate with partners



Basic Guidance from NIOSH

- **Updated and reissued in 2009**
- **Based on direct experience and applied research results**
- **Updated as new information is developed**
- **A starting point for building a responsible nanomaterial management program**

www.cdc.gov/niosh/topics/nanotech

Collaboration

- Share knowledge
- Use expertise
- Build experience
- Partner

The NIOSH Nanotechnology field team is available for site assessments, contact us.

The Nanotechnology Field Research Team Update

In 2006, NIOSH established a Nanotechnology Field Research Team to expand its knowledge and understanding of the potential health and safety risks that workers may encounter during the research, production, and use of engineered nanomaterials. This effort has complimented NIOSH's extensive laboratory-based research program, as well as helped NIOSH identify and more fully understand the variety of work processes used to generate and manufacture engineered nanomaterials. It has also provided NIOSH with the opportunity to observe and evaluate work practices and engineering controls used to ensure worker health and safety in the nanotechnology industry.

NIOSH has conducted site visits to several facilities around the country that are involved in the research, manufacture, or use of various types of nanomaterials including, metal and metal oxide nanoparticles, carbon nanofibers, electrospun nanofibers, quantum dots, fullerenes, and nanocomposites. As a result, NIOSH obtained valuable information that is being used to assist in developing workplace guidance documents to protect nanotechnology workers from occupational injury and illness, and has learned that:

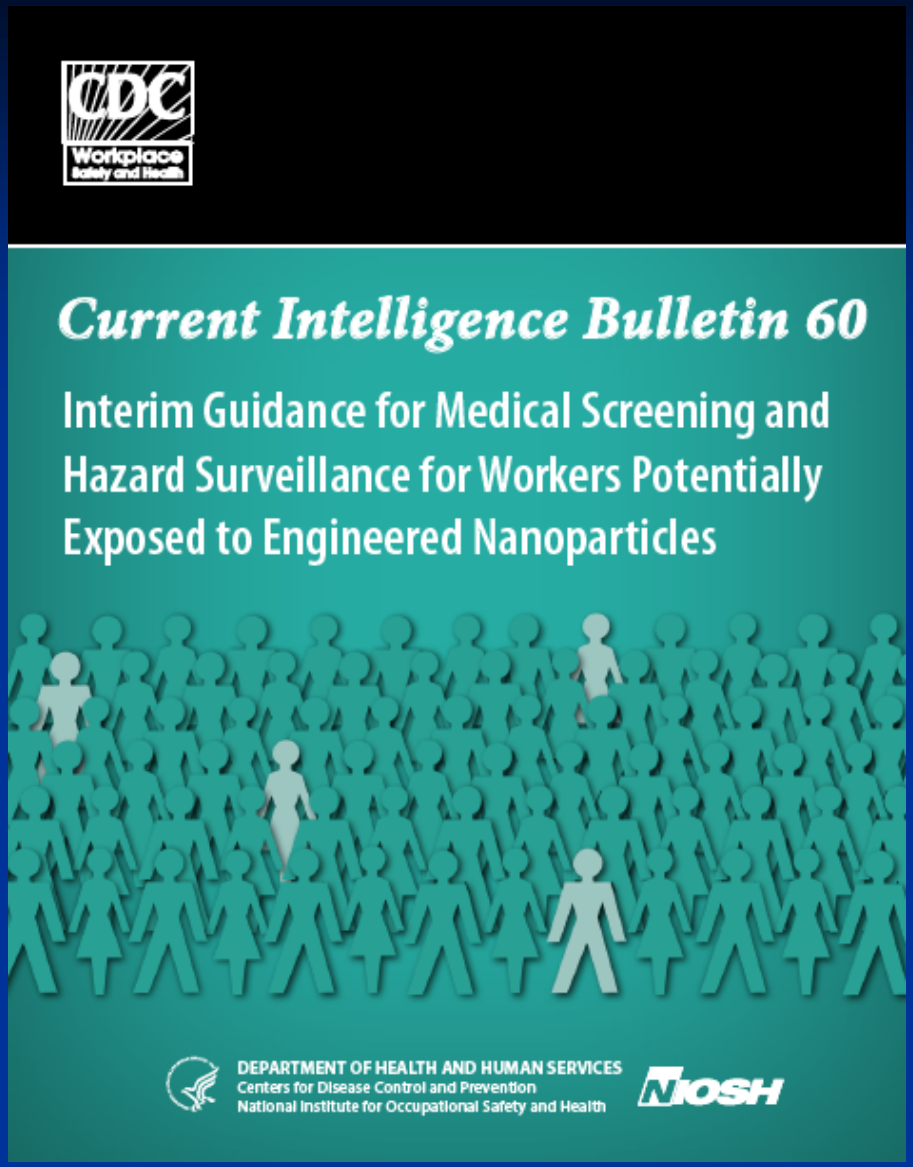
- basic particle counting and sizing instruments can be used to identify emissions from nanomaterial processes,
- careful interpretation of the particle data is needed to differentiate between incidental (background) and process-related nanoparticles, and
- engineering controls do minimize workplace exposure to engineered nanoparticles.

Companies interested in receiving a visit by the Field Research Team are encouraged to contact NIOSH. All site visits are initiated by the respective companies and are completely voluntary. This program is fully funded by NIOSH; therefore, there is no monetary cost to the participant. Three companies who have voluntarily received site evaluations from the NIOSH Field Research Team were recently interviewed by Nanowerk, LLC for its August/September 2007 issue of Nanorisk (www.nanorisk.org/). Overall, they described the collaboration as beneficial, and encouraged other companies to take advantage of NIOSH's expertise, services, instrumentation, and unbiased assessments.

For more information about occupational safety and health topics pertaining to engineered nanomaterials, including fact sheets about the Field Research effort and other nanotechnology research programs, please visit the NIOSH nanotechnology topic page at www.cdc.gov/niosh/topics/nanotech. To discuss the possibility of receiving a site evaluation by the NIOSH Field Research Team, contact Charles Geraci, Ph.D., CIH at (513) 533–8339, CGeraci@cdc.gov or Mark Methner, Ph.D., CIH at (513) 841–4325, MMethner@cdc.gov.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

NIOSH



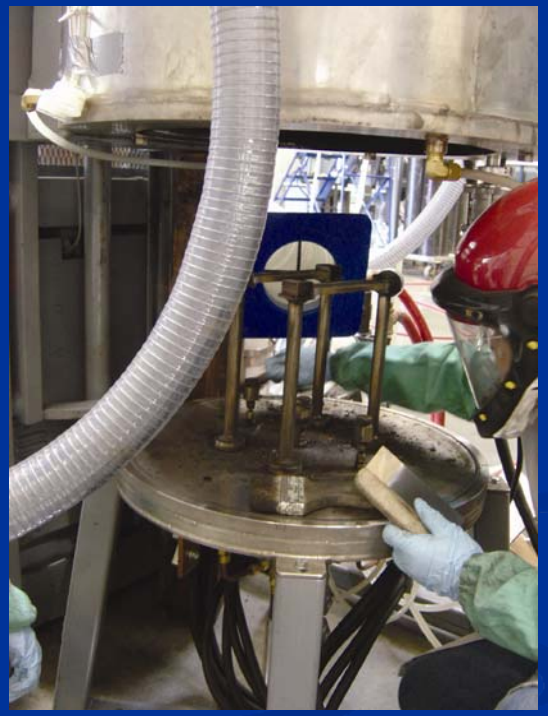
Interim guidance issued by NIOSH

Value of medical screening
Lack of specific health end point
Hazard Surveillance
Potential for Exposure Registry

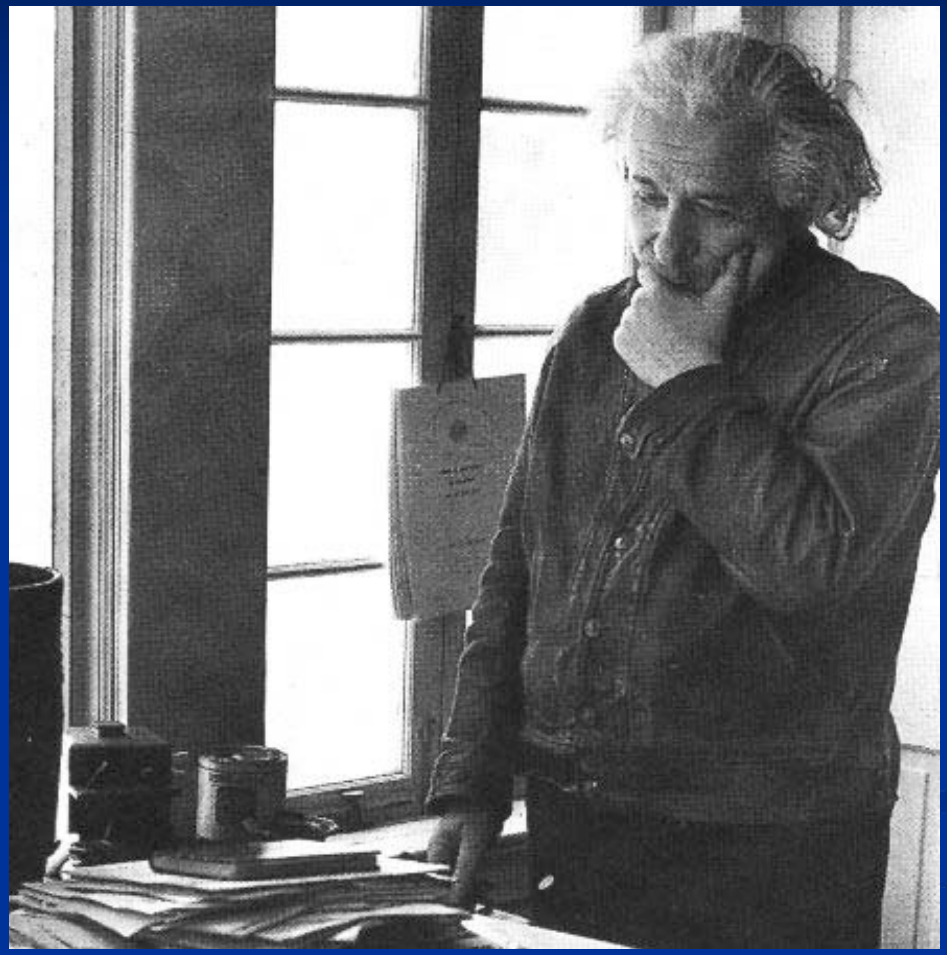
Nanotechnology: Summary

- More than 800 'nano' enabled products already in commerce.
- Hazards of nanomaterials are still not clear
- NIOSH is conducting research and developing guidelines on occupational exposures
- Research
  - Toxicology of nanoparticles
  - Measurement methods
  - Controls and worker protection
- Guidance
  - Exposure assessment
  - Control technologies
  - Medical screening and surveillance
  - Exposure registries
  - Epidemiologic studies

New
  - FR Notice: Information on CNTs



In the long term, nanotechnology may demand new thinking for occupational health and safety



In the short term, do what you already know.

There is still work to be done.

Thank you!

Charles.Geraci@cdc.hhs.gov